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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,043	02/04/2005	Paul Howley	23117	4403

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EXAMINER	
BLUMEL, BENJAMIN P	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/524,043	HOWLEY ET AL.	
	Examiner	Art Unit	
	Benjamin P. Blumel	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-26 and 28-31* is/are pending in the application.

4a) Of the above claim(s) *11-14,16,17 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,15,18-21,26 and 31* is/are rejected.

7)☒ Claim(s) *22-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 February 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/4/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I and the vaccinia virus host range gene C7L in the reply filed on October 11, 2006 is acknowledged. The traversal is on the ground(s) that the teachings of Fang et al. do not disclose a surprisingly high avipoxvirus titer. Therefore, applicants argue that Groups I-VI should be examined together due to a novel technical feature of the instant invention. However, this is not found persuasive because the claims of the instant application are not drawn to an avipoxvirus that can replicate to "surprisingly high titers" or other terminology that would convey to one in the art that such a novel technical feature exists in the claimed invention. Claims 1-9, 15, 18-26 and 31 will be examined in this Office action.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-14, 16, 17 and 28-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 11, 2006.

Claims 10 and 27 have been cancelled by applicant.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on February 4, 2005 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Objections

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The specification is objected to because the drawing descriptions for figures 4, 7A and 7B and the nucleic acid sequences on page 23 of the specification do not contain a specific SEQ ID No:. It is acknowledged that the drawing description for figure 4 does indicate SEQ ID NO: 1, but it is unclear if this SEQ ID NO: is specific for one of the nucleic acid sequences or the amino acid sequence present in the drawing. Furthermore, the specification refers to nucleic acids sequences by number. For example, on page 28, lines 8 and 9 of the specification, four primers are referred to as #496, #497, #505 and #506. Are these numbers meant to designate a specific nucleic acid sequence (i.e. an alternative for SEQ ID NO:) or are they meant to be merely a "name/title" for each primer? If these numbers are meant to designate a sequence, proper formate is required to comply with 37 CFR 1.821(a)(1) and (a)(2).

Applicants must comply with sequence rules in order to be considered a complete response to this Office Action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4-9, 15 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Tartaglia et al. (US 6,004,777).

The instant invention is drawn to a HIV vaccine comprising a recombinant avipoxvirus that expresses HIV antigens and contains the vaccinia host range gene K3L. The antigens expressed are *gag-pro*, gp120/TM, and Nef/Pol poly-epitope string. The presence of the K3L gene results in a replication competent avipoxvirus in cells. The avipoxvirus can either be a fowlpox or canarypox virus, however, if it is a canarypox virus then vaccinia virus E3L is not integrated. The vaccine of the instant invention is designed to produce an immune response in a human.

Tartaglia et al. disclose an immunological composition of recombinant poxviruses (fowlpox and canarypox) that express heterologous antigens, such as HIV antigens *gag-pro*, gp120/TM, and Nef/Pol poly-epitope string. Tartaglia et al. discuss the improved expression of heterologous antigens through the insertion of translation factors into the genome of recombinant poxviruses. The translation factors can be the open reading frames of: E3L, K3L, VAI RNA, EBER RNA, sigma 3, TRBP, a homolog thereof, and combinations thereof. Tartaglia et al. teach that the preferred translation factors are the Vaccinia E3L and K3L, which can be inserted in combination or separately into the recombinant poxvirus genome.

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Paoletti et al. (US 5,494,807).

The instant invention is drawn to an avian cell infected with an avipoxvirus and a vaccinia virus which contains at least one vaccinia virus host range gene or a homologue thereof.

Paoletti et al. teach the vaccination of mice with a vaccinia virus vaccine (NYVAC) and an avipoxvirus vaccine (ALVAC). Therefore, the presence of both vaccines *in vivo* would result in cells containing both viruses.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 15, 19, 26 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fang et al. (Virology, 2001), Tartaglia et al. *supra* and Perkus et al. (Virology, 1990).

The instant invention is drawn to a HIV vaccine comprising a recombinant avipoxvirus that expresses HIV antigens and contains the vaccinia virus host range genes K3L and C7L. The

antigens expressed are *gag-pro*, gp120/TM, and Nef/Pol poly-epitope string. The presence of the K3L and C7L genes result in a replication competent avipoxvirus in cells. The avipoxvirus can either be a fowlpox or canarypox virus, however, if it is a canarypox virus then vaccinia virus E3L is not integrated. The vaccine of the instant invention is designed to produce an immune response in a human.

Fang et al. teach the development vaccine composition of a recombinant avipoxivirus that expresses HIV antigens and is able to replicate in non-avian cells due to the presence of vaccinia virus E3L and K3L host range genes. Fang et al. utilize these genes in an attempt to elicit an beneficial immune response since the recombinant viruss replicated and expressed the HIV antigens *in vivo*. The antigens expressed by the recombinant canarypox virus were Gag, gp120/TM and Nef/Pol polyepitope string. Fang et al. do not teach the insertion of vaccinia virus host range gene C7L.

Tartaglia et al. as stated above, disclose the usage of vaccinia virus genes E3L and/or K3L in recombinant avipoxviruses to improve the expression of heterologous HIV antigens.

Perkus et al. teach the different host range genes of vaccinia virus and the effects each has on viral replication in non-avian cells. Either or both of the genes K1L and C7L of vaccinia virus are necessary for viral replication in human cells (MRC-5) as Perkus et al. observed no viral replication of the vaccinia virus double mutant in which K1L and C7L was deleted. However, the presence of either K1L or C7L genes resulted in a considerable titer following infection of MRC-5 and LLC-PK1 cells.

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Fang et al. and Tartaglia et al. in order to develop a recombinant avipoxvirus that

expresses HIV antigens and contains the host ranges C7L and K3L of vaccinia virus, thereby producing an immunological composition that can replicate in human cells. One would have been motivated to do so, given the suggestion by Fang et al. that vaccinia virus host range genes K3L and E3L or the suggestion by Tartaglia et al. that either or both of the K3L and E3L can be inserted into an avipoxvirus genome resulting in increased expression of viral nucleic acids and its replication in non-avian cells. There would have been a reasonable expectation of success, given the knowledge that host range gene C7L of vaccinia virus is necessary for viral replication in non-avian cells, as taught by Perkus et al. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 7-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant canarypox virus with the C7L vaccinia virus gene that can infect various eukaryotic cell lines, does not reasonably provide enablement for a HIV vaccine that contains the antigens Gag-pro, gp120/TM and Nef/pol polyepitope string expressed by a canarypox virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Nature of the invention. The claims are drawn to a vaccine for the treatment of HIV with an avipoxvirus with vaccinia virus host range gene K3L. The avipoxivirus has expression cassettes for HIV gag-pro, HIV gp 120/TM and HIV Nef/Pol poly-epitope string, respectively.

State of the prior art. At the time the invention was made, a vaccine for HIV was not known to exist. Furthermore, at the time of this Office Action, a vaccine for HIV is still not acknowledged in the art.

Breadth of the claims. The claims are broad, covering a vaccine for HIV.

Working examples. No working examples are disclosed in the specification with regard to a HIV vaccine. In fact, the only working example utilizing the claimed invention was the *in vitro* culturing of the recombinant canarypox virus with various eukaryotic cells. This example did not utilize a recombinant canarypox containing the K3L gene of vaccinia virus nor the HIV antigens claimed. The C7L vaccinia virus gene was the only heterologous gene of the claimed invention inserted into the recombinant virus.

Guidance in the specification. The specification provides guidance towards a recombinant avipoxvirus that contains HIV antigens Gag-pro, gp120/TM and Nef/Pol polyepitope string. However the effectiveness of the vaccine towards preventing or treating HIV is not discussed and no working examples exist related to the claimed invention, therefore, further guidance is required.

Predictability of the art. The art in general is acknowledged to be unpredictable (MPEP 2164.03). In the instant application, Applicants have not disclosed a functional vaccine for HIV, merely a recombinant canarypox virus that expresses marker genes and the C7L vaccinia virus

gene that is incubated with various eukaryotic cells. In addition, as stated above, as of the date in which this Office Action was written, no known HIV vaccine is recognized.

Amount of experimentation necessary. Since no working examples involving the claimed invention additional research is required to determine how effective the recombinant avipoxvirus as claimed would perform *in vivo*. Furthermore, experimentation has been on going towards the development of a HIV vaccine, however, as stated above, no known vaccine exists. The ability of HIV to mutate and incorporate its genome into the cell it infects, in addition to other tactics utilized by the virus to evade the immune system, have proven to be insurmountable for the scientific community. Therefore, further research is required for a greater understanding of what components could be effective against HIV.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Claims 18, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an avian cell that is co-infected with an avipoxvirus and a vaccinia virus which has at least one host range gene or a homologue thereof, does not reasonably provide enablement for an avian cell that is co-infected as stated above in addition to a recombinant canarypox virus that contains the host range gene K3L of vaccinia virus and the HIV antigens Gag-pro, gp120/TM and Nef/Pol polyepitope string or the integration of said host range gene into genome of the avian cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The factors above deemed most relevant are:

Guidance in the specification. The specification provides guidance towards a recombinant avipoxvirus that contains HIV antigens Gag-pro, gp120/TM and Nef/Pol polyepitope string. However the effectiveness of the vaccine towards preventing or treating HIV is not discussed and no working examples exist related to the claimed invention, therefore, further guidance is required.

Nature of the invention/ Breadth of the claims. The claims are drawn to an avian cell co-infected with any avipoxvirus and any vaccinia virus with at least one host range gene, an avipoxvirus that contains the K3L vaccinia virus gene and the expression cassettes for the HIV antigens Gag-pro, gp120/TM and Nef/Pol polyepitope string, in addition to the vaccinia virus gene K3L being integrated into the avian cell genome.

Working examples. No working examples are disclosed in the specification with regard to an avian cell co-infected with any avipoxvirus and any vaccinia virus with at least one host range gene, a recombinant avipoxvirus that contains the K3L vaccinia virus gene and the expression cassettes for the HIV antigens Gag-pro, gp120/TM and Nef/Pol polyepitope string in addition to the vaccinia virus gene K3L being integrated into the avian cell genome and being capable of infecting human cells. In fact, the only working example involved the *in vitro* culturing of a

recombinant canarypox virus with various eukaryotic cells. However, this example did not utilize the claimed recombinant canarypox invention since the only claimed heterologous gene inserted was the vaccinia virus C7L host range gene.

Claim Objections

Claims 1-8, 18-26 and 31 are objected to because of the following informalities: The present format of the above claims does not comply with MPEP § 608.01(m) because "the present Office practice is to insist that each claim must be the object of a sentence starting with "I (or we) claim," "The invention claimed is" (or the equivalent)". Appropriate correction is required.

Claims 22-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Summary

No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Benjamin P. Blumel whose telephone number is 571-272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Benjamin Blumel
Patent Examiner

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Notice to Comply	Application No. 10/524,043	Applicant(s) Howley et al.	
	Examiner Benjamin Blumel	Art Unit 1648	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The disclosure is missing SEQ ID NO:s, see attached Action under Objections.

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application.**

☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
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